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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/075,129 | 02/11/2002 | Patrick A. Tresco | 1094-1-011 | 8885 |
| 21552 | 7590 | 12/13/2004 | EXAMINER | |
| MADSON & METCALF GATEWAY TOWER WEST SUITE 900 15 WEST SOUTH TEMPLE SALT LAKE CITY, UT 84101 | | | NAFF, DAVID M | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1651 | |
| DATE MAILED: 12/13/2004 | | | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

| | | |
|-----------------|---------------|--|
| Application No. | Applicant(s) | |
| 10/075,129 | TRESCO ET AL. | |
| Examiner | Art Unit | |
| David M. Naff | 1651 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM
THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 30 September 2004.
2a) This action is **FINAL**. 2b) This action is non-final.
3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-37 is/are pending in the application.
4a) Of the above claim(s) 22-25 and 27-30 is/are withdrawn from consideration.
5) Claim(s) _____ is/are allowed.
6) Claim(s) 1-21,26 and 31-37 is/are rejected.
7) Claim(s) _____ is/are objected to.
8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
 Paper No(s)/Mail Date _____
- 4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date. _____
5) Notice of Informal Patent Application (PTO-152)
6) Other: _____

DETAILED ACTION

In a response of 9/30/04 to a restriction requirement of 8/25/04, applicants amended claims 22 and 26-28, and elected Group I claims 1-21 and 31-37 with traverse.

5 The traverse is on the ground that claims 22 and 26-28 have been amended to require the structural features of claim 1, thus the methods of Groups II, III and IV cannot be performed without the device of Group I. In view of the amendments, the restriction between Groups I and III is withdrawn, and Group III claim 26 will be examined 10 with Group I claims 1-21 and 31-37. The amendments do not obviate restriction of the claims of Groups II and IV. The device and methods of Groups I and III can be used *in vitro* whereas Group II claims 22-25 are drawn to an *in vivo* process due to a step c of implanting. Group 15 IV claims 27-30 require a step c of incubating with a different type of cells that does not have to occur when using the device and methods of the claims of Groups I and III. Additionally, the Group IV claims require a combination of oriented surface roughness and surface curvature not required by the claims of Groups I, II and III, and the claims of Group IV do not require implanting a composite resulting 20 from a step b as in the claims of Group II, and recovering tissue from a step c as in the claim of invention III.

For the reasons above, the restriction is maintained except that Groups I and III are combined, and the restriction requirement is made final.

Claims 22-25 and 27-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5 9/30/04.

Claims examined on the merits are 1-21, 26 and 31-37.

Applicant is advised that should claims 1-7 and 33-37 be found allowable, claims 8-15 and 33-37 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an 10 application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 8-15 and 33-37 require the same device as claims 1-7 and 15 33-37. A difference in the preambles of claims 1 and 8 does not make the devices different.

Applicant is advised that should claim 12 be found allowable, claim 13 will be objected to under 37 CFR 1.75 as being a substantial 20 duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

There is no difference in claims 12 and 13.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C.

112:

5 The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21, 26 and 31-37 are rejected under 35 U.S.C. 112,

second paragraph, as being indefinite for failing to particularly

10 point out and distinctly claim the subject matter which applicant regards as the invention.

In line 5 of claim 1 and where required in other claims,

"cytoskeletal elements aligned uniformly" is uncertain as to meaning and scope. It is uncertain as to material that constitutes

15 cytoskeletal elements, and the relationship of these elements to the cells in of a first layer. It is further uncertain as to position of the elements that constitutes being aligned uniformly since no element structure capable of being aligned is required.

In line 7 of claim 1 and where required in other claims, "layer

20 oriented in the direction of said first layer" is uncertain as to meaning and scope since the first layer has not been required to be oriented in a direction.

In lines 5 and 6 of claim 1 and where required in other claims,

requiring the bioartificial composite to act as a template to accept a 25 second layer of cells upon the first layer is unclear as to the difference in the first and second layers since how the second layer is produced has not been specified.

In claim 2 and where required in other claims, it is uncertain as to how "at least 200 nm root mean squared" defines surface roughness. What physical feature of roughness does at least 200 nm root mean squared define, and how would one know when roughness is at least 200 nm root mean squared? What physical characteristics of roughness are measured and calculations made to determine when the roughness is at least 200 nm root mean squared?

In claim 3 and where required in other claims, it is uncertain as to how "equal or greater than .016 microns⁻¹" defines surface curvature. How would one know when surface curvature is equal or greater than .016 microns⁻¹? What surface dimension is measured and calculations made to determine the claimed surface curvature?

Claims 16-18 are unclear as to whether the substrate being further limited is that of claim 8 or some other substrate. If the 15 claims are further limiting the substrate of claim 8, the claims should refer specifically to the substrate of claim 8 and define how the substrate is further limited.

Claims 19 and 20 are confusing and unclear as to structure of the device required by describing only an isolated portion of the 20 structure and failing to describe sufficient structure for a complete device to be clear how the claimed structure is combined with other structure to form a complete device. In line 2 of claim 19, it is uncertain as to structure required when the substrate of the bioartificial composite defines an axially aligned surface topography, and how this structure relates to the surface and first layer of claim

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8. There is not clear antecedent basis for "the long axis" (line 4) and "the free upper surface of said first layer" (line 5). It is unclear as to the relationship of the layer of cells attached to said molecules in line 3 to the first and second layers of cells in claim

5 8. Is the second cell layer in line 5 the second layer of cells in claim 8 or is this an additional second layer? It is unclear as to whether the second cell layer in line 5 is intended to be attached to the free upper surface, or is it intended to be capable of being attached to the free upper surface. The meaning of cells "that

10 attached" to the free upper surface in line 5 is unclear.

In lines 5 and 6 of claim 19 and line 1 of claim 20, "morphological rearrangement" is uncertain as to meaning and scope. Rearrangement that is morphological is relative and subjective, and dependent on how one defines morphological rearrangement.

15 In claim 5, and where required in other claims "over all non-planar shape" is uncertain as to meaning and scope. An over all non-planar shape would be relative and subjective.

In line 3 of claim 20, it is uncertain as to what constitutes "force" on said first layer and/or said substrate. Does this mean 20 that one presses an object or material against the layer and/or substrate, or does this mean that some other force is applied? It is not seen how any force can promote rearrangement, and how applying a force to the substrate and not the cells can promote rearrangement.

Claim 21 is unclear by requiring in the preamble producing the 25 device of claim 1 or 8 and requiring steps that appear to produce only

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the substrate in claim 1 or 8. Producing only the substrate will not produce the device since there is more to the device than just the substrate.

In claims 4 and 11, it is uncertain as to structural features

5 that constitute a repeating surface structure. Does a repeating surface structure mean multiple surfaces having structures, or does this have some other meaning?

Claim 31 is confusing by requiring cells from a "host" since the meaning and scope of "host" is uncertain, and it would be uncertain as 10 to cells that are from a host and not from a host.

In claim 32, there is not clear antecedent basis for "the implant" and "said platform".

In claim 36, the abbreviation "CNS" is confusing due to its meaning not being readily apparent. The full name should be recited.

15 In claim 37, --- from the group consisting of --- should be inserted after "selected" in line 1 and in line 2, --- and --- should be inserted before "dorsal" to set forth a proper Markush group and be clear.

Claim Rejections - 35 USC § 102

20 The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

25 (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 8-13, 21 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Clark et al.

The claims are drawn to a device for propagation of tissue comprising a bioartificial composite comprising a substrate having at 5 least one surface capable of the reception and growth of promoting retention of a cellular preparation and a first layer of adherent cells prepared from the preparation disposed on the surface. The first layer has cytoskeletal elements aligned uniformly, and the composite serves as a template to accept a second layer of cells upon 10 the first layer. The second layer comprises an organized layer oriented in the direction of the first layer, and the substrate has at least one surface defined by a critical surface curvature and/or topography. Also claimed is a method of preparing the device.

Clark et al disclose topographical guidance of cells using 15 multiple grooved substrata to obtain aligned cells thereon.

The grooved substrata containing aligned cells of Clark et al is a device that is the same as the device presently claimed. The cells on the substrata of Clark et al are inherently in the form of a layer having cytoskeletal elements aligned uniformly, and the layer is 20 inherently capable of serving as a template for a second layer of cells as claimed. The substrata of Clark et al inherently has a critical surface curvature and/or topography. The conditions of dependent claims are also inherently part of the substrata containing cells of Clark et al. The method of preparing the device of Clark et 25 al is the same as required by claim 21.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

5 (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention 15 was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art 20 under 35 U.S.C. 103(a).

20

Claims 1-19, 21, 26 and 31-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naughton et al (5,858,721) in view of Clark 25 et al and Ricci et al (6,419,491 B1) and Curtis et al (4,832,759).

25

The invention is described above. Additionally, claim 26 requires a method for preparation of tissue by incubating the substrate containing a layer of cells.

30

Naughton et al disclose (paragraph bridging cols 2 and 3, and col 3, lines 9-25) growing stromal cells on a support matrix to produce a

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stromal matrix and then growing cells derived from a desired tissue on the stromal matrix to produce components of tissue analogous to counter parts found *in vivo*. Multiple cell layers are provided (col 6, line 36).

5 Clark et al is described above.

Ricci et al disclose (col 4, lines 36-49) a dental implant having a collar section containing an ordered microgeometric repetitive surface pattern in the form or a multiplicity of alternating ridges and grooves that define a guide for preferential promotion of the 10 rate, orientation and direction of growth colonies of cells.

Curtis et al disclose (col 1, lines 26-37) locating a plurality of cells in a predetermined spatial disposition relative to each other on a solid substrate by providing a generally planar surface with discontinuities defining cell-adhesion enhanced and/or cell-adhesion 15 orienting zones. The discontinuities can be grooves and ridges (col 2, lines 5-10). The cells can be cells having cytoskeletons (col 2, lines 28-37).

It would have been obvious provide the support matrix of Naughton et al with features such as grooves and/or ridges to provide 20 topographical cell guidance as suggested by Clark et al and to promote orientation and direction of cell growth as suggested by Ricci et al and to provide cells in a predetermined spatial disposition as suggested by Curtis et al. Naughton et al disclose multiple layers being obtained, and the stromal cells form a first layer and the 25 tissue-specific cells form a second layer, and the stromal layer

inherently acts as a template for the second layer. The conditions of dependent claims would have been matters of obvious choice in view of the disclosures of the references. Naughton et al disclose (col 3, lines 22-26, and col 8, lines 48-52) treating the matrix with 5 materials to enhance cell attachment as in claims 6 and 7, and these materials will inherently minimize non-specific protein binding. A substrate with a roughness or curvature as in claim 2 or 3 and non-planar shape as in claim 5 would have been obvious from roughness and curvature of the substrates of Clark et al, Ricci et al and Curtis et 10 al. A filamentous substrate as in claim 16, cylindrical substrate as in claims 17 and 18 and an axially aligned surface topography as in claim 19 would have been merely a matter of individual preference for a particular form and/or shape of the substrate. The support of Naughton et al can have cell attachment molecules as in claim 19. The 15 method of claim 21 is suggested by Clark et al, and producing tissue as in claim 26 would have been obvious from the tissue producing method of Naughton et al. Cell sources and forms of substrate as in claims 31-37 would have been obvious from cells and substrates from disclosed by the references.

20 **Claim Rejections - 35 USC § 103**

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-19, 21, 26 and 31-37 above, and further in view of Vandenburg (4,940,853).

25 The claim requires applying force to the layer of cells or substrate to promote morphological rearrangement.

Vandenburgh discloses that it is known to apply forces to align cells when producing tissue (col 1, lines 20-25).

When forming tissue by the method of Naughton et al and using a support matrix as set forth above, it would have been obvious to apply 5 force to align cells in tissue produced as suggested by Vandenburgh.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be 10 reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for 5 unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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David M. Naff
Primary Examiner
Art Unit 1651

DMN
12/9/04